

## ORIGINAL ARTICLE

# COMPARATIVE STUDY BETWEEN BOTULINIUM TOXIN INJECTION AND PARTIAL DIVISION OF PUBORECTALIS FOR TREATING ANISMUS

By

Hesham A Moneim, Waleed Omar, Tarek Mahdy, Mohamed Farid

Colorectal Surgery Unit, Mansoura University Hospital, Egypt

Correspondence to: Hesham A Moneim, Email: dhesham\_moneim@yahoo.com

**Aim:** to compare the results of partial division of puborectalis (PDPR) versus local botulinum toxin (BTX-A) injection in treating patients with anismus.

**Methods:** this prospective randomized study included 30 male patients with a mean age  $38.93 \pm 12.39$  years and a mean duration of  $5.80 \pm 3.96$  years. Diagnosis was made by clinical examination, barium enema, colonoscopy, colonic transit time, anorectal manometry, balloon expulsion test, defecography, and EMG. Patients were randomized into: Group (I): included 15 patients injected with BTX-A, and Group (II): included 15 patients who underwent bilateral PDPR. Follow up was conducted for one year.

**Results:** Both BTX-A and PDPR significantly reduced the preoperative constipation scores. The initial and long term success rates were 86.7% and 40% in BTX-A group versus 100% and 66.6% in PDPR group. Recurrence was observed in 7 patients (53.8%) and 5 patients (33.4%) following BTX-A and PDPR respectively. Minor incontinence had occurred in 2 patients (13.3%) following PDPR.

**Conclusion:** BTX-A injection seems to be successful for temporary treatment of anismus. However, PDPR has been found to be a promising method for treatment of anismus with a relatively lower morbidity in relation to its higher success rate.

**Keywords:** Puborectalis syndrome, obstructed defecation, maladaptive constipation.

## INTRODUCTION

Anismus is a behavioral disorder in which there is failure of relaxation or even a paradoxical contraction of the puborectalis muscle during attempted defecation.<sup>(1)</sup>

Patients almost complain of prolonged straining, inability to initiate defecation, feeling of incomplete evacuation, need for manual disimpaction, laxative or enema abuse, as well as rectal pain.<sup>(2)</sup>

Diagnosis of anismus is aided by anal manometry,<sup>(3)</sup> balloon expulsion test,<sup>(4)</sup> electromyography (EMG) of the external anal sphincter and puborectalis muscle,<sup>(5)</sup> colon

transit time<sup>(6)</sup> and defecography.<sup>(7)</sup> Unfortunately, no single test has been conclusive in determining the presence of anismus.<sup>(8)</sup>

Management usually starts with high residue diets to elicit rectal voiding followed by the use of increasing doses of laxatives and enemas with no effect in solving the problem.

Biofeedback training has been used for treating anismus patients with conflicting results.<sup>(9,10)</sup>

A wide variety of surgical and pharmacologic approaches have been proposed, with the aim of eliciting puborectalis muscle relaxation.<sup>(1)</sup>

The aim of this prospective randomized study was to compare the results of partial division of puborectalis versus local botulinium toxin injection in treating patients with anismus.

## PATIENTS AND METHODS

This study comprised a prospective randomized study of 30 patients with outlet obstruction due to anismus. They were referred to our Colorectal Surgery Unit, Mansoura University Hospital during the period from September 2003 to September 2005.

They were 30 males, with a mean age  $38.93 \pm 12.39$  years (range, 20-69 years). Mean duration of constipation was  $5.80 \pm 3.96$  years (range, 1-20 years). All patients fulfilled the Rome II criteria (2 or more of the following) for constipation:

- History of long-standing constipation (>12 months)
- Straining in more than one-quarter of defecations
- Lumpy or hard stools in more than one-quarter of defecations
- Sensation of incomplete evacuation in more than one-quarter of defecations
- Sensation of anorectal obstruction / blockage in more than one-quarter of defecations
- Manual maneuvers to facilitate more than one-quarter of defecations
- Less than three defecations per week.<sup>(11)</sup>

Diagnosis of anismus was made by clinical examination, barium enema, colonoscopy, colonic transit time, anorectal manometry,<sup>(9)</sup> Balloon expulsion test,<sup>(12)</sup> defecography,<sup>(13)</sup> and electromyography (EMG) of the puborectalis muscle.<sup>(14)</sup>

### *The inclusion criteria were:*

- Fulfilling Rome II symptomatic criteria for functional constipation.
- 4 positive functional tests for anismus of anal manometry, EMG, defecography, balloon expulsion test and physical examination of pelvic floor muscle during defecation.
- There must be an evidence for inappropriate contraction or failure to relax the pelvic floor muscle during attempts to defecate in at least 4 of these tests.
- There must be an evidence of adequate propulsive forces during attempts to defecate (rectal pressure > 45 mm hg).
- Incomplete, prolonged and difficult evacuation, with constant use of enema, laxatives and digital evacuation,

in spite of having a regular and sometimes daily urge to defecate.

*The Exclusion criteria were:* Sphincteric defects, colonic inertia, defecographic abnormalities other than anismus (e.g. rectocele), previous pelvic surgery as well as pregnancy.

After careful explanation of the clinical condition and the options of treatment, our patients signed informed consents. Then, patients were then randomized through a computer generated series of consecutively numbered, sealed envelopes into 2 groups:

### • *Group I patients (Botulinium toxin "BTX-A" injection):*

It included 15 male patients. Their age ranged from 20 - 63 years (mean  $34.73 \pm 12.33$  years).

All of them were injected with BTX- A. The toxin was injected while patients were in the left lateral position. A vial of Dysport, 500 u, (Dysport, Ipsen, United Kingdom) was dissolved in 2.5 ml isotonic saline. A volume of 0.5 ml of dissolved toxin (100 u Dysport), was injected in each patient. The injection was given with an insulin syringe fitted to a needle size of 21 gauze and 3.75 cm in length. The needle tip was guided by the contra lateral index finger into the anal canal. BTX- A was injected into the left and right sides of the paradoxically contracting puborectalis and the external anal sphincter at 5 and 7 o'clock in lithotomy position. This procedure was done as an outpatient procedure.

### • *Group II patients (Bilateral open partial division of puborectalis):*

It consisted of 15 male patients, with age ranging from 24 - 53 years (mean  $38.26 \pm 8.01$  years).

All of them were subjected to open bilateral partial division of the puborectalis (PDPR). Each patient was admitted to the hospital and subjected to routine preoperative medical assessment. In the operating room, and while patients under general anesthesia and in lithotomy position, a 2-3 cm curved incision is made on either side of the anal canal along its postero-lateral aspect, each about 2.5 cm distance from the anal verge. Dissection through the ischio-rectal fossa till the puborectalis sling was reached. Using a right angle forceps, the puborectalis sling was lifted up, and nearly the inner half of puborectalis sling was divided on each side by using a scalpel No. 11.

Complete haemostasis followed by skin closure was carried out without a drain. Post operative wound care in the form of daily dressing and oral antibiotics (metronidazole and ciprofloxacin) were given for five days.

Patients were followed up for a mean period of  $14.73 \pm 4.54$

months (ranged from 6-24 months). It was conducted weekly in the first month then every 2 weeks in the second month then monthly thereafter.

At each visit, patients were assessed regarding the improvement in bowel habits and PR examination to assess the relaxation of puborectalis muscle during straining. Patients were asked to fulfill a symptom questionnaire of Mansoura for constipation one month following the therapeutic procedure and again at the end of the follow up.

By this questionnaire the degree of improvement was assessed as regarding the straining severity, anorectal pain, number of weekly bowel movements, sensation of incomplete evacuation and need for anal digitations or enema.

The term clinical improvement or success was chosen to reflect the patients who returned to normal bowel habits experienced by the patient long time ago before the disease.

Patients were assessed one month after the procedure by anorectal manometry, balloon expulsion test, defecography and EMG examination of the anal sphincter to monitor any changes in paradoxical contraction and to show whether the clinical improvement was associated with normalization of objective findings or not.

Any degree of post operative incontinence was assessed by using Mansoura scoring system for incontinence with (A) means incontinence to flatus, (B) incontinence to mucous, (C) incontinence to liquid stool and (D) incontinence to solid stool. Each grade may be 1 (once / week) or 2 (> once / week) or 3 (> once / day).

Recurrence after initial improvement was assessed by defecography to detect the cause of recurrence.

The statistical analysis of the data in this study was preformed using the SPSS version 11 under windows XP. The tests used were the Arithmetic mean value (average) and standard deviation, Frequency (percentage), Student's t test (a P value < 0.05 was considered significant) and Chi-square test.

## RESULTS

From September 2003 to September 2005, a group of 30 patients complaining of anismus were randomly divided into two groups.

**Group I** included 15 male patients with a mean age  $34.73 \pm 12.33$  years and a mean disease duration  $5.93 \pm 3.28$  years. All patients in group (I), were injected by botulinium toxin type A (BTX-A).

**Group II** included 15 male patients with a mean age  $38.26 \pm 8.01$  years and a mean disease duration  $5.67 \pm 4.66$  years. All patients in group (II) underwent bilateral open partial

division of puborectalis muscle (PDPR).

Slow transit constipation was recorded in 2 patients in group (I) and in 3 patients in group II Table 1.

**Table 1. Demographic profile of our patients.**

		BTX-A	PDPR
Age (years)	Range	20.0 - 63.0	24.0 - 53.0
	Mean $\pm$ SD	$34.73 \pm 12.33$	$38.26 \pm 8.01$
Disease duration (years)	Range	2.0 - 12.0	1.00 - 20.0
	Mean $\pm$ SD	$5.93 \pm 3.28$	$5.67 \pm 4.66$
Slow transit time		2 (13.3%)	3 (20%)

Both botulinium toxin injection and PDPR significantly reduced the preoperative constipation score that persisted till the end of the follow up period Table 2.

**Table 2. Comparison between pre-operative/injection and post-operative/injection constipation scores in our patients.**

	Pre-op/inj.	Early Post-op/inj.	Late-op/inj.	Student t-test	
				Pre-op/inj. vs. Early post-op/inj.	Pre-op/inj. vs. Late post-op/inj.
Group I	$11.20 \pm 0.94$	$5.00 \pm 2.10$	$8.20 \pm 2.57$	0.0001	0.0001
Group II	$11.40 \pm 0.74$	$2.27 \pm 1.62$	$6.13 \pm 1.69$	0.0001	0.0001

However, we found that PDPR was more effective in reducing the constipation score, both early and late, than BTX-A injection Table 3.

**Table 3. Comparison of Constipation score (early and late) following BTX-A and partial division of puborectalis.**

	BTX-A	PDPR	Student t test	
			T	P
Constipation score (early)	5 ± 2.10	2.27 ± 1.62	3.98	0.0004
Constipation score (late)	8.2 ± 2.57	6.13 ± 1.68	2.61	0.015

As regards the manometric parameters, we found that BTX-A injection significantly reduced the mean pressure during straining (MPDS) with no other significant changes in the manometric parameters. This was in contrast to PDPR which produced a significant postoperative reduction in mean resting pressure of the upper anal canal (MSU), mean squeeze upper (MSU), functional anal canal length (FACL) and in mean pressure during straining (MPD S) Table 4.

**Table 4. Comparison between pre and post-injection /operative motility studies in our patients.**

	Pre-injection	Post-injection	Student t test	
			T	P
<b>Group I:</b>				
MRU	77.33 ± 6.51	76.60 ± 6.01	0.32	0.75
MSU	174.47 ± 26.14	163.46 ± 23.94	1.20	0.24
MRL	76.67 ± 6.55	79.33 ± 5.49	-1.20	0.23
MSL	172.80 ± 24.89	175.06 ± 25.27	-0.24	0.80
FAC length	3.95 ± 0.42	3.80 ± .43	0.94	0.35
MPDS	108.27 ± 11.70	76.47 ± 10.72	7.76	0.0001
<b>Group II:</b>				
MRU	82.666 ± 9.839	71.733 ± 7.950	3.34	0.002
MSU	188.133 ± 44.949	149.133 ± 32.808	2.71	0.011
MRL	79.866 ± 5.730	83.866 ± 6.022	-1.86	0.073
MSL	172.333 ± 30.960	177.666 ± 32.358	-0.46	0.64
FAC length	3.9200 ± .6073	3.4067 ± .5161	2.76	0.01
MPDS	112.466 ± 22.369	66.866 ± 8.983	7.32	0.0001

There was a significant difference in the diagnostic utilities findings before and after BTX-A injection and also before and after partial division of puborectalis Table 5.

**Table 5. Comparison between pre-inj/op and post-inj/op. diagnostic utilities in treated groups.**

	Paradox.	Group I				Group II			
		Pre-inj	Post-inj	X2	P	Preop.	Postop	X2	P
EMG	Paradox.	15 (100%)	2 (13.3 %)	22.9	0.0001	14 (99.3%)	2 (13.3%)	19.286	0.0001
	Non-paradox.	0 (0 %)	13 (86.7 %)			1 (6.7 %)	13 (86.7%)		
Defecogram	+ve	14 (93.3%)	2 (13.3 %)	19.286	0.0001	13 (86.7 %)	0 (0.0 %)	22.94	0.0001
	-ve	1 (6.7 %)	13 (86.7 %)			2 (13.3 %)	15 (100%)		
Balloon ET	Retained	15 (100 %)	3 (20.0 %)	20.00	0.0001	15 (100%)	2 (13.3 %)	22.94	0.0001
	Expelled	0 (0.0 %)	12 (80.0 %)			0 (0.0 %)	13 (86.7 %)		
PR	+ve	15 (100 %)	2 (13.3 %)	22.94	0.0001	15 (100%)	0 (0.0 %)	30.00	0.0001
	-ve	0 (0.0 %)	13 (86.7 %)			0 (0.0 %)	15 (100%)		

Botulinium toxin injection achieved initial improvement or success in 13 patients (86.7%). However, long term success recorded at the end of follow up, persisted only in 6

patients (40%). This was in contrast to PDPR which achieved initial improvement or success in all patients (100 %) with a long term success in 10 patients (66.6%).

Recurrence of symptoms of obstructed defecation was recorded in 7 patients (53.8%) following BTX-A injection. The cause of recurrence in these patients was the recurrence of anismus. In PDPR, recurrence of symptoms due to obstructed defecation was observed in 5 patients (33.4%), in 4 of them, the cause of recurrence was rectal intussusception and in one, the cause of the recurrence was anismus.

No complications were recorded following BTX-A injection. Complications following partial division of puborectalis were in the form of wound disruption and infection in 10 patients (66.7 %). These patients were treated by daily dressing and antibiotics till wound healing had achieved. 2 patients (13.3%) developed mild incontinence for flatus with one grading (A1) and the other was in the form of soiling once / week (B1). Rectal intussusception was recorded in 4 patients (26.7%) following open division.

At the end of our follow up, 10 & 6 patients (66.7% & 40.0%) were found satisfied following PDPR and BTX-A injection respectively. However, this difference did not produce any significant value (P=0.14) Table 6.

**Table 6. Comparison of patients' satisfaction following BTX-A injection and partial division of puborectalis.**

	BTX-A injection	Partial division of puborectalis	Chi-square test	
			X2	P
Patient satisfaction	6(40.0 %)	10 (66.7 %)	02.14	0.14

## DISCUSSION

Treatment of anismus is quite disappointing. Several surgical techniques have been described for dividing the puborectalis muscle in patients with constipation who have paradoxical contraction. Although initial results were satisfactory,<sup>(15,16)</sup> Subsequent results were very disappointing and resulted in high rates of incontinence.<sup>(17-19)</sup> These results pushed several investigators to consider surgery has no role in the therapeutic approach of anismus should be considered as a last resort for treating these patients.<sup>(20-22)</sup>

A recently described non surgical alternative is injection of clostridium botulinum type A (BTX-A) neurotoxin directly into the puborectalis muscle.<sup>(23)</sup> BTX-A is a potent neurotoxin that causes paralysis of muscles by presynaptic inhibition of acetylcholine release.<sup>(24)</sup>

Hence this study came to revive the results of partial

division of puborectalis muscle and to compare its results with botulinium toxin injection.

All patients in our study were males. This is in contrast to Preston and Lennard-Jones (1985) and Duthie & Bartolo (1992) who especially described anismus in young or middle aged women.<sup>(25,26)</sup> This difference could be explained by social factors in our community as female, especially of low education level, are always reluctant to seek medical advice. Actually, in Egypt, no epidemiologic data exists on the prevalence of anismus or sex difference.

Several authors reported that botulinium toxin seemed to be a promising treatment for patients with anismus, but repeated injections might be necessary to maintain clinical improvement.<sup>(20,27,28)</sup>

In our series, BTX-A injection significantly decreased the preoperative constipation score that continued till the end of our follow up. Complete clinical improvement was recorded in 13 patients (86.7%) following injection and persisted only in 6 patients (40%) with recurrence of symptoms in 7(46.7%) patients. Our results differed from those reported by Ron et al. (2001) who observed only 37.5% success after the first injection.<sup>(29)</sup>

Maria et al. (2000) used an EMG guided technique for exact location of the puborectalis muscle,<sup>(20)</sup> while Hallen et al. (1988) reported that this technique proved unnecessary.<sup>(23)</sup> Also, Shafik and Sibai (1998) reported that the puborectalis could be identified by per-rectal examination.<sup>(28)</sup>

In our study, endoanal ultrasound was not of help in guiding injection and we found that finger guidance was a simple clinical tool for accurate localization of the puborectalis.

Hallen et al. (1988) used the British form of BTX-A and reported that incontinence had occurred in 2 cases in their series.<sup>(23)</sup> In our study, we used the British form of BTX-A (Dysport, Ipsen, United Kingdom) in which each nanogram contained 40 mouse units. The complications of injection such as fecal incontinence, local infection or bleeding were not observed. Our results coped with those obtained by Madalinski et al. (2002) who injected 16 patients suffering from anismus and recorded only minor complications in the form of pain and intertrigo.<sup>(30)</sup>

Furthermore, bilateral PDPR significantly decreased the preoperative constipation score in patients in group II and this decrease remained significant till the end of our follow up. Complete clinical improvement was recorded in all of 15 patients (100%) following the operation and this clinical improvement persisted only in 10 patients (66.7 %). Recurrence of symptoms had occurred in 5 patients (33.3%). The cause of recurrence was rectal intussusception in 4 patients and recurrence of anismus in one patient. So

that, bilateral partial division of puborectalis seemed to be a promising method for treatment of anismus with initial success rate reaching 100% percent and long term success reaching 66.7%.

Postoperative complications following PDPR were in the form of wound infection and/or disruption in 10 patients (66.7%), incontinence in 2 patients (13.3%) both patients were incontinent only to flatus with one had a grade A1 and the other grade A2 incontinence. Rectal intussusception was recorded in 4 patients.

Our results are similar to those of Wasserman (1964) who described surgical division of part of puborectalis muscle and reported good results (success rate 100%).<sup>(15)</sup> Our results are also in accordance with Wallace and Madden (1969) who reported a large series of anismus patients to whom PDPR was carried out with apparently good results.<sup>(16)</sup>

Barnes et al. (1985) reported nine women with anismus who were treated by posterior division of puborectalis muscle with a success rate 22.2% and incontinence rate 55.5%. They explained that failure rate to be related to disruption of the anorectal anatomy by previous anorectal or pelvic surgeries that might impair rectal contractility or disturb the normal defecatory reflexes.<sup>(18)</sup>

In our series, we excluded any patient with previous pelvic or rectal surgery and this may partially explain the difference in success rates between our results and those of Barnes et al 1985.<sup>(18)</sup>

Regarding the manometric findings, BTX-A injection did not produce any significant changes except in the mean pressure during straining ( $P = 0.001$ ). On the contrary, partial division of puborectalis produced a significant decrease in the mean resting upper, mean squeeze upper, functional anal canal length and mean pressure during straining.

Our findings were similar to Maria et al. (2000) who reported that there was a significant decrease in the anal tone during straining following BTX-A injection, whereas, anal resting pressure and maximum voluntary contraction were unchanged.<sup>(20)</sup>

In our study, there were significant changes in the results of EMG, defecography, balloon expulsion test and per rectal examination ( $P < 0.001$ ) one month after BTX-A injection or partial division of puborectalis. This may indicate that subjective results goes with the objective results and also may indicate the efficacy of both methods in treating anismus.

Patient satisfaction from the procedures is an important factor deciding the success of any procedure. In our series 10 patients were satisfied by the results of partial division

at the end of follow up. This is in contrast to only 6 patients following BTX-A injection. However this difference failed to reach a significant value ( $p=0.14$ ).

BTX-A injection seems to be successful for temporary treatment of anismus. However, bilateral partial division of puborectalis has found to be a promising method for treating patients suffering from anismus. It has a relatively lower morbidity in contrast to its higher success rate.

## REFERENCES

1. Whitehead WE, Wald A, Diamant NE, Enck P, Pemberton JH. Functional disorders of the anus and rectum. *Gut*. 1999;45:1155-9.
2. Kuijpers HC, Bleijenberg G. The spastic pelvic floor syndrome: a cause of constipation. *Dis Colon Rectum*. 1985;28:669-72.
3. Weber, J., Ducrotte, P. H., Touchais, J. Y., Roussigno, C., Denis, R. N. Biofeedback training for constipation in adults and children. *Diseases of the Colon and Rectum*. 1987;30:844-6.
4. Preston DM, Lennard-Jones JE. Anismus in chronic constipation. *Dig Dis Sci*. 1985;30:413-18.
5. Johansson C, Nilsson BY, Mellgren A, Dolk A, Holmstrom B. Paradoxical sphincter reaction and associated colorectal disorders. *Int J Colorectal Dis*. 1992;7:89-94.
6. Wexner SD, Cheape JD, Jorge JM, Heymen S, Jagelman PG. Prospective assessment of biofeedback for the treatment of paradoxical puborectalis syndrome. *Dis Colon Rectum*. 1992;35:145-50.
7. Kuijpers HC, Bleijenberg G, de Morree H. The spastic pelvic floor syndrome. Large bowel outlet obstruction caused by pelvic floor dysfunction: a radiological study. *Int J Colorectal Dis*. 1986;1:44-8.
8. Schouten WR, Briel JW, Auwerda JJA, van Dam JH, Gosselink MJ, Ginai AZ, et al. Anismus: fact or fiction? *Dis Colon Rectum*. 1997;40:1033-41.
9. Park UC, Choi SK, Piccirillo MF, Verzaro R, Wexner SD. Patterns of anismus and the relation to biofeedback therapy. *Dis. Colon Rectum*. 1996;39:768-73.
10. Gilliland, R., Heymen, S., Altomare, D. F., Park, U. C., Vickers, D., & Wexner, S. D. Outcome and predictors of success of biofeedback for constipation. *Br J Surg*. 1997;84:1123-6.
11. Thompson WG, Longstreth GF, Drossman DA, Heaton KW, Irvine EJ, et al. Functional bowel disorders and functional abdominal pain. *Gut*. 1999;45:II43-II4.
12. Pemberton JH, Rath DM, Ilstrup M. Evaluation and surgical treatment of severe chronic constipation. *Ann Surg*. 1991;214:403-13.

13. Halligan S, Bartram C, Park HJ, Kamm M. Proctographic features of anismus. *Radiology*. 1995;197:679-82.
14. Halverson AL, Orkin BA. Which physiologic tests are useful in patients with constipation? *Dis. Colon Rectum*. 1998;41:735-9.
15. Wasserman JF. Puborectalis syndrome: Rectal stenosis due to anorectal spasm. *Dis Colon Rectum*. 1964;7:87-98.
16. Wallace WC, Madden WM.: Experience with partial resection of the puborectalis muscle. *Dis Colon Rectum*. 1969;12:196-200.
17. Keighley MRB, Shouler P. Anorectal outlet syndrome: Is there a surgical option? *JR Soc Med*. 1984;77:559-563.
18. Barnes PR, Hawley PR, Preston DM, Lennard-Jones JE. Experience of posterior division of the puborectalis muscle in the management of chronic constipation. *Br J Surg*. 1985;72:475-7.
19. Kamm MA, Hawely PR, Lennard-Jones JE. Lateral division of puborectalis muscle in the management of severe constipation. *Br.J. Surg*. 1988;75:661-3.
20. Maria G, Brisinda G, Bentivoglio AR, Cassetta E, Albanese A. Botulinum toxin in the treatment of outlet obstruction constipation caused by puborectalis syndrome. *Dis Colon Rectum*. 2000;43:376-80.
21. Rao SS. Constipation: evaluation and treatment. *Gastroenterol. Clin. North Am*. 2003;32:659-83.
22. Andromanakos N, Skandalakis P, Troupis T, Filippou D. Constipation of anorectal outlet obstruction: Pathophysiology, evaluation and management. *J Gastroenterol and Hepatol*. 2006;21:638-46.
23. Hallan RI, William NS, Melling J, Waldron DJ, Womack NR, Morrison JF. Treatment of anismus in intractable constipation with botulinum A toxin. *Lancet*. 1988;2:714-7.
24. Jankovic J and Brin MF. Therapeutic uses of botulinum toxins. *N Engl Med*. 1991;324:1186-94.
25. Preston DM, Lennard-Jones JE. Anismus in chronic constipation. *Dig Dis Sci*. 1985;30:413-18.
26. Duthie GS, Bartolo DCC. Anismus: The cause of constipation? Results of investigation and treatment. *World J Surg*. 1992;16:831-5.
27. Joo JS, Agachan F, Wolff B, Nogueras JJ, Wexner SD. Initial North American experience with botulinum toxin Type A for treatment of anismus. *Dis Colon Rectum*. 1996;39:1107-11.
28. Shafik A, El-Sibai O.: Botulinum toxin in the treatment of nonrelaxing puborectalis syndrome. *Dig Surg*. 1998;15:347-51.
29. Ron Y, Avni Y, Lukovetski A, Wardi J, Geva D, Birkenfeld S, Halpern Z.: Botulinum toxin type-A in therapy of patients with anismus. *Dis Colon Rectum*. 2001;44:1821-6.
30. Madalinski MH, Slawek J, Duzynski W, Zbytek B, Jagiello K, Adrich Z, et al. : Side effects of botulinum toxin injection for benign anal disorders *Eur J Gastroenterol Hepatol*. 2002;14:853-6.